1. THE OFFICE ACTION

The March 4, 2009 Office Action (the "Office Action") in this application a) rejected claims 1, 4, 5 and 8 and new claim 14 on the ground of non-statutory obviousness-type double patenting; and b) rejected claims 1, 4, 5, 8 and 14 under 35 U.S.C. 103(a). Applicant respectfully traverses these rejections.

2. CLAIM REJECTIONS – DOUBLE PATENTING

The Office Action has rejected claims 1, 4, 5 and 8 and new claim 14 on the grounds of non-statutory obviousness-type double patenting over claims 1-5, 7-15 and 18 in U.S. Patent 6,383,509. Applicants respectfully traverse these rejections. However and solely in order to expedite prosecution, and without acquiescing to the propriety of this double patenting rejection, a Terminal Disclaimer over U.S. patent 6,383,509 is hereby enclosed. In accordance with MPEP 804.02, the filing of this and previously submitted terminal disclaimers to obviate the rejections based on nonstatutory double patenting is not an admission of the propriety of the rejection. *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991). In accordance with the submission of this Terminal Disclaimer over U.S. U.S. Patent 6,383,509, the instant rejection is thus rendered moot. Accordingly, reconsideration and withdrawal of the rejection is requested.

3. Claim Rejections – 35 U.S.C 103

The Office Action has rejected claims 1, 4, 5, 8 and 14 under 35 U.S.C 103(a) as being unpatentable over Singh et al. (USP 66994859) and Aoki et al. (USP 6113915). Applicant respectfully traverses this rejection.

It is noted that Singh et al. specifically disclose the isolation and purification of the Hn-33 polypeptide ***from*** Clostridium botulinum neurotoxin complexes (col. 1, lines 53-55; col. 2, lines 11-15; col. 2, line 25; col. 3, lines 47-51; col. 3, lines 64-66; col. 4, lines 55-57; col. 5, lines 4-5; col. 6, lines 43-46); or its production by transformation of a host cell with an Hn-33-encoding DNA fragment (col. 5, lines 7-17). Singh et al. disclose isolation of Hn-33 from botulinum toxin, for example, from botulinum toxin type A and type E (col. 10, lines 34-36; Example 1

(cols 13-15). The Figures of this reference also disclosed the isolation of Hn-33, as shown and described. As stated clearly in the detailed description, "The invention relates to isolated, biologically active, protease resistant hemagglutinin polypeptides from the type A *Clostridium botulinum* neurotoxin complex, referred herein as Hn-33" (col. 3, lines 64-67).

Additionally, it is stated at col. 22, lines 16-21, that the compositions of Singh et al. (containing the Hn-33 protein isolated from the naturally occurring botulinum toxin complexes) are "..useful for patients requiring more neurotoxic activity or less administered drug due to the side-effects caused by non-neurotoxin ingredients". Thus, and properly constructing this reference as a whole, the principle of operation of this invention is based on the isolation and use of Hn-33 *from* botulinum toxin complexes. Furthermore, by specifically teaching the isolation and use of Hn-33, Singh et al. specifically teaches away from the use of native neurotoxin complexes, with their host of non-neurotoxin proteins, from which and in accordance with this disclosure, the compositions of Singh et al. (including Hn-33) are isolated from.

The Office Action states (Office Action of March 4, 2009, on page 4, third paragraph) that "One of ordinary skill in the art, at the time the invention was made, would have been motivated to use the botulinum toxin complexes that are released by the various Clostridium botulinum types A-F in the composition an method of Singh et al. because Aoki et al. teach that the intact botulinum toxin complexes provide stability and have a slower rate of diffusion within an intramuscular site. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation for combining the botulinum neurotoxins of Aoki et al. with the composition and method of Singh et al. because Singh et al. teach the inclusion of any botulinum neurotoxin in the complex,...".

Respectfully, such a holding is untenable and flies in the face of what the whole point of Singh et al. reference teaches and is based upon, namely, the isolation and use of Hn-33 *from* botulinum toxin complexes, and in some instances combined with the neurotoxin molecule. Respectfully, a botulinum neurotoxin complex is made up of a neurotoxic component (having a molecular weight of about 150 kDa) and non-toxin complex proteins (e.g. Hn-33). In other words, the principle of operation in Singh et al. is based on the isolation and use of the hemagglutinin protein Hn-33 *from* botulinum toxin complexes. The Office Action's suggested

modification of Singh et al., by the addition of whole complexes of Aoki et al. to the compositions of Singh et al., does not comport with the principle of operation of Singh et al., that is, the removal and use of Hn-33 *from* the complexes (i.e. it would in essence bring Sing et al. back to square one, i.e., the composition is no longer the isolated and purified Hn-33 polypeptide *from* Clostridium botulinum neurotoxin complexes, but rather includes the neurotoxin complexes as wholes).

Respectfully, in accordance with MPEP 2143.01, "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 and further, "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). Here, the Office Action's proposed modification of essentially adding back/utilizing whole botulinum toxin complexes (having weights of 300kDa, 500 kDa, 900 kDa) which are the staring points for and from which resistant hemagglutinin polypeptides are isolated (e.g. Hn-33) and the compositions of Singh et al., is simply a suggested modification that renders Singh et al. as being modified unsatisfactory for its intended purpose (see e.g. , col. 22, lines 16-21) and further would change the principle of operation of Singh et al., that is, utilized complex proteins from which the compositions of Singh et al. (containing Hn-33) are *isolated* from. Thus, the Office Action has clearly not made a proper prima facie showing of obviousness and the instant rejection is respectfully request to be withdrawn.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) month extension of time for filing a reply in connection with the outstanding office action.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Claude L. Nassif at the telephone number below, in order to expedite prosecution in connection with the present application.

The Commissioner is hereby authorized to charge any fee(s) required or necessary for the filing, processing or entering of this paper or any of the enclosed papers (including extension of time fees and Terminal Disclaimer fees) and to refund any overpayment to deposit account 01-0885.

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Respectfully submitted,

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